بسم الله الرحمن الرحيم

شبكة المعلومـــــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

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SYNTHESIS AND SPECTRAL STUDIES ON HETEROCYCLIC NITROGEN COMPOUNDS

Thesis

Submitted for the degree of (Ph.D.)

BY

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SUMMARY

Summary

Heterocyclic rings, like triazolines, quinazolines, oxazolidines, thiazoles, benzoxazoles, oxazines and oxadiazines are reported to exhibit biological activity. The aim of this work was:

(1) The use of p-N-succinimidobenzoyl isothiocyanate to prepare these heterocycles substituted with pyrrolidine dione hopping to enhance their biological activity.

(ii) The use of α-cyano-β-phenylcinnamoyl isothiocyanate as a start for the synthesis of oxazine, pyrimidine as well as quinazoline system. All these systems are substituted with a cyano group and this is expected to increase their biological activity.

Part I

p-N-succinimidobenzoyl isothiocyanate (I) was prepared from its acid chloride by treating its solution in acetone with ammonium thiocyanate. The isothiocyanate obtained in *situ* was used in heterocyclic synthesis.

Treatment of (I) with phenyl hydrazine afforded 2-phenyl-1-H-3-(p-N-succinimidophenyl)- Δ^3-1,2,4-triazoline-5-thione (V).

Reaction with aroyl hydrazine e.g. benzoylhydrazine and p-chlorobenzoyl hydrazine gave thiosemicarbazide derivatives (VIIa-b), which have been used as precursors to synthesize 3-aryl-4-(p-N-succinimidobenzoyl)-Δ^2-1,2,4-triazoline-thiones (VIIIa,b) by cyclization using polyphosphoric acid.

When isothiocyanate (I) was treated with anthranilic acid, the diaryl thiourea derivative (IX) was obtained, the latter was converted to 3-(p-N-succinimidobenzoyl)-1,3-quinazolin-4-one-2-thione (X) by refluxing in acetic anhydride.

Reaction of (I) with glycine produced an equilibrium mixture of the diaryl thiourea (XI) and 2-(p-N-succinimidobenzamide)-2-thiol-1,3-oxazolidine-5-one (XII).

Treatment of (I) with thioglycollic acid, followed by heating with acetic anhydride produced 3-(p-N-succinimidobenzoyl)-1,3-thiazolidine-5-one-2-thione (XIV).

Thiocarbamate derivative (XV), produced from the reaction of o-aminophenol with isothiocyanate (I) was converted upon fusion to 2-N-(p-N-succinimidobenzamide)-1,3-benzoxazole (XVI).

Cyanoacetamide condenses with isothiocyanate (I), leading to the formation of 2-(p-N-succinimidophenyl)-5-carboxamido-6- isopropylid-enamino-4-H-1,3-oxazin-4-thione(XVIII).

Finally, guanidine reacts with isothiocyanate (I) producing a mixture of 6-amino-4-(p-N-succinimidophenyl)-1,3,5-triazin-2-thione (XIX) and 6-isopropylidinamino-2-(p-N-succinimidophenyl)-1,3,5-oxadiazin-4-thione (XX).

In addition to the above mentioned heterocycles our interest to synthesise biologically active compounds was extented to the synthesis of thiourea derivatives (XXIa-c) through the reaction of isothiocyanate (I)

with aromatic amines, as well as the synthesis of thiocarbamates (XXII) by reaction of (I) with ethanol.

All the above mentioned compounds were proved by extensive spectral studies using I.R, ^{1}H. NMR as well as a detailed study of their mass spectra.

Part II

α-cyano-β- phenylcinnamoyl isothiocyanate (XXV) was prepared from α-cyano-β-phenylcinnamoylchloride by treatment with ammonium thiocyanate. When treated with water, 5-cyano-6,6-diphenyl-oxazin-4-one-2-thione (XXVI) was produced.

Reaction of (XXV) with benzoylhydrazine produces 1-(N-benzamido)- 5- cyano-6,6-diphenyl-pyrimidin-4-one-2-thione (XXVIII).

The synthesis of 1-aryl-5-cyano-6,6-diphenyl-hexahydro-pyrimidin-4-one-2-thione (XXXa-c), was through the reaction of isothiocyanate (XXV) with aromatic amines.

Reaction of (XXV) with anthranilic acid yields the diaryl thiourea (XXXIII) used as a precursor in the synthesis of-3-[α-cyano-β. phenylcinnamoyl]quinazolin-4-one-2-thione (XXXV) or quinazolin-4-one-2-thione (XXXIV) by treatment of (XXXIII) with acetic anhydride for different reaction periods.

The structure of all the prepared compounds was proved by elemental analysis, I.R, ^{1}H. NMR and mass spectra.

INTRODUCTION